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PATENT LEGAL DEPARTMENT/A-42-C
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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,308	REDDY ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-13,15,18,20-25,27,29,32-34 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-13,15,18,20-25,27,29,32-34 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed June 29, 2006 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 1, 2, 4-13, 15, 18, 20-25, 27, 29 and 32-34 were pending. Applicants added claim 37 and amended claims 1, 5, 7, 8, 11, 12, 18, 20, 21, 22, 24, 27, 29 and 32. Therefore, claims 1, 2, 4-13, 15, 18, 20-25, 27, 29, 32-34 and 37 are currently pending and examined on the merits.

Withdrawn Objections/Rejections

4. The objection to claim 11 is withdrawn in view of Applicants' amendment to claim 11. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 102

5. Claims 1, 2, 9, 12, 13, 18, 29 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Jennissen et al. (Jennissen et al., "Biocoating of Implants with Mediator Molecules: Surface Enhancement of Metals by Treatment with Chromosulfuric Acid" Mat.-wiss. u. Werkstofftech. 1999, 30, 838-845) as evidenced by Madsen (Madsen, N. B. "Modification and

characterization of the interface in polymer/inorganic composites" Risø National Laboratory, 1999, pages 3-6) and Zumbrink et al. (Zumbrink, et al. "Analysis of Affinity Supports by 13C CP/MAS NMR spectroscopy: Application to Carbonyldiimidazole- and Novel Tresyl Chloride-Synthesized Agarose and Silica Gels" Journal of Molecular Recognition, 1995, 8, 363-373) and Bethell et al. (Bethell et al., "A Novel Method of Activation of Cross-linked Agaroses with 1,1'-Carbonyldiimidazole which Gives a Matrix for Affinity of Chromatography Devoid of Additional Charged Groups" J. Biol. Chem. 1979, 254(8), 2572-2574) and FDA (U.S. Food and Drug Administration "InFuse™ Bond Graft/LT-CAGE™ Lumbar tapered Fusion Device – P000058" September 2002, pages 1-3, accessed from http://www.fda.gov/cdrh/mda/docs/p000058.pdf).

For ***claims 1 and 12***, Jennissen et al. (see entire document) disclose biocoating of implants with mediator molecules (e.g., see Jennissen et al., abstract), which anticipates the claimed invention. For example, Jennissen et al. disclose (a) providing a solid support consisting essentially of an organic polymer having at least one available amino group including solid supports selected from the group consisting of plates and films (e.g., see page 840, last paragraph wherein Ti-APS is disclosed; see also page 840, column 2, paragraph 2 wherein "plates" are disclosed). In this scenario, the one available amino group is the terminal amine of the APS and the organic polymer is the cross-linked APS that is bound to the titanium solid support. The reference doesn't explicitly state that APS forms an organic polymer, but the Examiner contends that Jennissen et al. inherently discloses this feature as evidenced by Madsen (e.g., see Madsen, page 5, figure 1.2 showing polymerization of organosilanes and their subsequent attachment to free

hydroxyl groups; see also Jennissen et al., page 840, column 2, paragraph 1). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). In addition, Jennissen et al. disclose (b) reacting the available amino group on the solid support with an activating compound, the activating compound having the structure L_1-X-L_2 as defined in the claim so that the reaction results in L1 being displaced by the available amino group on the solid support to form an activated support (e.g., see page 840, column 2, paragraph 2 wherein CDI is used to form Ti-APS-CDI plates; CDI falls within the scope of L_1-X-L_2 when L_1 and L_2 are aryl and X is -C(=O)-). Jennissen et al. also disclose (c)-(d) providing a biological molecule having at least one reactive amino, thiol or hydroxyl group, the biological molecule being a macromolecule selected from the group consisting of nucleic acids, polypeptides chains and carbohydrates and reacting the biological molecule with the activated support, thereby displacing L2 and covalently attaching the biological molecule to the solid support so that the biological molecule is available for use in an assay (e.g., see page 840, column 2, last paragraph wherein ubiquitin is used to form Ti-APS-CDI-ubiquitin plates; see also page 841, column 1, paragraph 1 wherein rhBMP is used to form Ti-APS-CDI-rhBMP plates). Please note that the limitation "available for use in an assay" has not been afforded any patentable weight because it

represents mere "intended" use language. See In re Pearson, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974); In re Yanush, 477 F.2d 958, 959, 177 USPQ 705, 706 (CCPA 1973); In re Casey, 370 F.2d 576, 580, 152 USPQ 235, 238 (CCPA 1967); In re Stencel, 828 F.2d 751, 754, 4 USPQ2d 1071, 1073 (Fed. Cir. 1987); In re Venezia, 530 F.2d 956, 958-59, 189 USPQ 149, 152 (CCPA 1976).

For ***claims 2 and 13***, Jennissen et al. disclose imidazole (e.g., see page 841, column 1, paragraph 1 wherein CDI is disclosed).

For ***claim 9***, Jennissen et al. do not explicitly disclose the use of an organic solvent but, instead, refer to the Zumbrink and Bethell publications for the CDI reaction conditions, which do disclose the use of organic solvents like dioxane (e.g., see page Jennissen et al., page 840, column 2, paragraph 1, "... activation by CDI [was accomplished] as described for Silica gel [14] [which refers to the Zumbrink reference]"; see also Zumbrink Materials and Methods and figure 4 which in turn refers to the Bethell et al. reference; see also Bethell et al., page 2572, Material and Methods which disclose the use of dioxane for activation).

For ***claim 18***, Jennissen et al. also disclose a washing step (e.g., see page 840, column 2, paragraph 2).

For ***claim 29***, Jennissen et al. do not explicitly state that they use a hormone, therapeutic drug or drug of abuse, but a therapeutic drug is inherently disclosed by Jennissen et al. as evidenced by the FDA, which provided approval for BMP-2 in treating degenerative disc disease (e.g., see Jennissen et al., page 838, abstract wherein BMP-2 is disclosed; see also FDA, page 1 wherein BMP-2 is approved to treat degenerative disc

disease).

For ***claims 12 and 32***, Jennissen et al. disclose a plate or film (e.g., see page 840, last paragraph wherein Ti-APS is disclosed; see also page 840, column 2, paragraph 2 wherein "plates" are disclosed).

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that Jennissen et al. do not provide a solid support "consisting essentially of" an organic polymer having at least one available amino group as set forth in newly amended claims 1, 12 and 29 (e.g., see 6/29/06 Response, page 12, section IV).

This is not found persuasive for the following reasons:

The Examiner respectfully disagrees. MPEP § 211.03 states, "For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase 'consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention.")." Here, the

specification does not set forth a "clear indication" what the basic and novel characteristics are and, as a result, the term "consisting essentially of" has been interpreted as "comprising" in accordance with MPEP § 211.03. For example, Applicants state:

> Solid supports capable of having an available amino group attached thereto include a wide range of materials including but not limited to natural materials and synthetic materials. Natural materials include but are not limited to cellulose, and agarose. Synthetic materials include but are not limited to polypropylene, polystyrene, polymethacrylate, nylon [i.e., organic polymers]. The solid supports used in the invention may take different forms such as a bead, plate, film, or other structures. Procedures for providing a solid support with an available amino group are well known in the art, and an example of a procedure is described in U.S. Pat. No. 5,112,736 which is incorporated by reference herein.

(e.g., see specification, page 6, third full paragraph). Thus, Applicants provide no "clear indication" how the "organic polymers" should be limited. To the contrary, Applicants state that "a wide range of materials" may be used that are "not limited to natural materials and synthetic materials" (see above). In addition, Applicants state that the solid supports can take many different forms including the use of "plates", which reads on the plates disclosed by Jennissen. Therefore, Applicants' arguments are moot.

Alternatively, the Examiner contends the solid supports disclosed by Jennissen do not "materially affect the basic and novel characteristic" and, as a result, anticipate the "consisting essentially of" limitation in accordance with MPEP § 211.03. The only possible "basic and novel" characteristic of the claimed solid supports is that they all contain a "free amino group" (whether they're made from an organic polymer or not), which is exactly what Jennissen et al. disclose (see rejection above). That is, the underlying Ti does not inhibit the availability of the free amino groups in the organic polymer. Therefore, even if, assuming arguendo, Applicants' "consisting essentially of" language could be fairly construed more narrowly (which is not the case, see above), Jennissen et al. would still anticipate the claim.

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

Claim Rejections - 35 USC § 103

7. Claims 1, 2, 4, 9-13, 15, 18, 29, 32 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jennissen et al. (Jennissen et al., "Biocoating of Implants with Mediator Molecules: Surface Enhancement of Metals by Treatment with Chromosulfuric Acid" Mat.-wiss. u. Werkstofftech. 1999, 30, 838-845) in view of Stolowitz et al. (WO 87/06586) (Date of Publication is November 5, 1987) (of record) as evidenced by Madsen (Madsen, N. B. "Modification and characterization of the interface in polymer/inorganic composites" Risø National Laboratory, 1999, pages 3-6) and Zumbrink et al. (Zumbrink, et al. "Analysis of Affinity Supports by 13C CP/MAS NMR spectroscopy: Application to Carbonyldiimidazole- and Novel Tresyl Chloride-Synthesized Agarose and Silica Gels" Journal of Molecular Recognition, 1995, 8, 363-373) and Bethell et al. (Bethell et al., "A Novel Method of Activation of Cross-linked Agaroses with 1,1'-Carbonyldiimidazole which Gives a Matrix for Affinity of Chromatography Devoid of Additional Charged Groups" J. Biol. Chem. 1979, 254(8), 2572-2574) and FDA (U.S. Food and Drug Administration "InFuse™ Bond Graft/LT-CAGE™ Lumbar tapered Fusion Device – P000058" September 2002, pages 1-3, accessed from http://www.fda.gov/cdrh/mda/docs/p000058.pdf).

For ***claims 1, 2, 9, 12, 13, 18, 29 and 32***, Jennissen et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 1, 2, 9, 12, 13, 18, 29 and 32.

The prior art teaching of Jennissen et al. differ from the claimed invention as follows:

For ***claims 4, 15 and 37***, Jennissen et al. fail to disclose the use of 1,2,4-carbonyl di-triazole.

For ***claim 10***, Jennissen et al. fail to disclose the use of an organic base.

For ***claim 11***, Jennissen et al. fail to disclose aqueous conditions.

However, Stolowitz et al. teach the following limitations that are deficient in Jennissen et al.:

For ***claims 4, 15 and 37***, Stolowitz et al. disclose, for example, 1,2,4-carbonyl di-triazole (e.g., see Stolowitz et al., page 10, paragraph 1, "A variety of azolides other ... may be employed ... include[ing] N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonyldiindole, N,N,-carbonylidibenzimidazole and N,N'-carbonyldibenztriazole and others"; see also Stolowitz et al., abstract; see also page 9, formula 7 wherein the urea linkage is shown; see also Summary of Invention, "In addition, a number of important specific objectives are also achieved using the present invention, including: The use of N,N'-carbonyldiimidazole for the activation of a chromatographic support with other than pendant hydroxyl groups; The preparation of a urea derivative of a bonded phase chromatographic support and the unique hydrophilic nature of the urea linkage"; see also Example 1, lines 8-18; see also page 3, lines 14-20; see also page 3, lines 21-26).

For ***claim 10***, Stolowitz et al. disclose, for example, triethylamine (e.g., see Example 1).

For ***claim 11***, Stolowitz et al. disclose both aqueous and organic conditions (e.g., see Summary of Invention, "Derivatization results from reaction of the activated support with a functionalizing reagent consisting of a primary or secondary, alkyl or aryl amine in organic solvent, or from an aqueous solution of the amine or its salt").

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use 1,2,4-carbonyl di-triazole as disclosed by Stolowitz et al. to immobilize BMP-2 as disclosed by Jennissen et al. because Stolowitz explicitly states that 1,2,4-carbonyl di-triazole can be used as a substituted for CDI in similar types of coupling reactions (e.g., see Stolowitz et al., page 10, paragraph 1, "A variety of azolides other than N,N'-carbonyl-diimidazole [i.e., the coupling agent used by Jennissen] may be employed ... include[ing] N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonyldiindole, N,N,-carbonylidibenzimidazole and N,N'-carbonyldibenztriazole and others."). A person of skill in the art would have been motivated to use such a coupling reagent because the coupling reagents have similar structures and exhibit very similar properties to CDI (e.g., see page 10, paragraphs 1-2). Stolowitz et al. also state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30) and that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35; see also Stolowitz et al., page 4, lines 23-25). In addition, Stolowitz et al. state that their method provides for a physical barrier that enhances the efficiency of the chromatographic procedures (e.g., see Stolowitz et al.,

page 4, lines 11-19, "The preparation of a physical barrier preventing interaction between surface silanols and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and sample components) and that the "urea" linkage has favorable properties (e.g., see Stolowitz et al., page, 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the residual silanol activity beneath it"). Finally, a person of skill in the art would have reasonably expected to be successful because Stolowitz et al. shows the use of 1,2,4-carbonyl di-triazole in a coupling reaction involving aminopropyl silica gel (e.g., see abstract; see also Summary of Invention; see also Examples) which is exactly the same reaction disclosed by Jennissen et al. (e.g., see Jennissen et al., column 2, paragraph 1). In addition, Stolowitz et al. also state, "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35).

Alternatively, the Examiner contends that Stolowitz et al. stands for the proposition that CDI and 1,2,4-carbonyl di-triazole represent "equivalent" coupling reagents (e.g., see Stolowitz et al., page 10, paragraph 1 as outlined above) and, as a result, motivation to substitute one for another need not be provided. See in In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982) ("Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious").

Response

8. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue that Jennissen et al. is not "analogous art" because the present claims are directed to "use in an assay" (e.g., see newly amended claim 1) whereas Jennison's invention was directed to coating bone implantable metals with biologically active molecules (e.g., see 6/29/06 response, pages 12 and 13, especially page 13, paragraph 1).

[2] Applicants argue that there is no motivation to combine because the Stolowitz reference is "so far removed from" the field of endeavor of Jennison et al. that no motivation could presumably could possible exist (e.g., see 6/29/06 response, pages 13 and 14).

[3] Applicants argue that the references "discredit" each other in some way and cite In re Young in support of this position (e.g., see 6/29/06 Response, pages 14 and 15). Although Applicants' arguments are less than clear, Applicants note that Stolowitz teaches that non-specific interactions are problematic for chromatographic applications (e.g., see 6/29/06 Response, page 14, last paragraph) and that Jennison et al. provide evidence of specific non-specific absorption (e.g., see 6/29/06 Response, page 15, paragraph 1) which, presumably, would discourage a person of skill in the art from combining said references.

[4] Applicants argue that Stolowitz merely provides and "obvious to try" rationale and cite In re O'Farrell in support of this position (e.g., see 6/29/06 Response, paragraph bridging pages 15 and 16).

[5] Applicants argue that the combined references only teach solid supports "consisting essentially of" inorganic materials (e.g., see 6/29/06 Response, page 16, second to last paragraph).

[6] Applicants argue that the combined references don't teach the "available for use in an assay" limitation (e.g., see 6/29/06 Response, page 16, last paragraph).

This is not found persuasive for the following reasons:

[1,6] The Examiner respectfully disagrees. The phrase "so that the biological molecule is available for use in an assay" has not been afforded any patentable weight because it represents mere "intended use" language. See In re Pearson, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974); In re Yanush, 477 F.2d 958, 959, 177 USPQ 705, 706 (CCPA 1973); In re Casey, 370 F.2d 576, 580, 152 USPQ 235, 238 (CCPA 1967). Whether a statement in a claim of purpose or intended use constitutes a limitation for purposes of patentability must be determined by the facts of each case in view of the claimed invention as a whole. See In re Stencel, 828 F.2d 751, 754, 4 USPQ2d 1071, 1073 (Fed. Cir. 1987). Furthermore, intended use language that describes a "future condition" which may or may not later happen is not generally afforded patentable weight. See In re Venezia, 530 F.2d 956, 958-59, 189 USPQ 149, 152 (CCPA 1976). Here, the phrase "so that the biological molecule is available for use in an assay" describes a "future" condition that may or may not happen. That is, the newly amended claim only requires that attached biological molecule be "available" for use in an assay at some "future" date. Consequently the phase "so that the biological molecule is available for use in an assay" does not constitute a patentable limitation. Therefore, the claims are not limited to the "assay" field of invention as erroneously purported. Consequently, Applicants' non-analogous arguments are

moot.

[2] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the present case, a person of skill in the art would have been motivated to use such a coupling reagent because the coupling reagents have similar structures and exhibit very similar properties to CDI (e.g., see page 10, paragraphs 1-2). Stolowitz et al. also state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30) and that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35; see also Stolowitz et al., page 4, lines 23-25). In addition, Stolowitz et al. state that their method provides for a physical barrier that enhances the efficiency of the chromatographic procedures (e.g., see Stolowitz et al., page 4, lines 11-19, "The preparation of a physical barrier preventing interaction between surface silanols and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and sample components) and that the "urea" linkage has favorable properties (e.g., see Stolowitz et al., page, 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the residual silanol activity beneath it"). Finally, a person of skill in the art

would have reasonably expected to be successful because Stolowitz et al. shows the use of 1,2,4-carbonyl di-triazole in a coupling reaction involving aminopropyl silica gel (e.g., see abstract; see also Summary of Invention; see also Examples) which is exactly the same reaction disclosed by Jennissen et al. (e.g., see Jennissen et al., column 2, paragraph 1). In addition, Stolowitz et al. also state, "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35).

With regard to Applicants non-analogous art comment (i.e., "so far removed from" the field of endeavor), the Examiner notes that coupling reactions are not "unique" to the field of biocompatible implants as exemplified in Jennissen and, as a result, a person of ordinary skill in the art would have looked to other areas such as chromatography wherein ligands were routinely bond to solid supports. See In re Paulsen 31 USPQ2d 1671 (Fed. Cir. 1994) (A "clam style" fastening means is not "unique" to the computer industry and, as a result, a person of skill would consult other "mechanical" literature for a solution to this fastening problem).

[3] The test to determine if a reference "teaches away" is to determine if one "would be discouraged from following the path set out in the reference, or would be lead in a direction divergent from the path that was taken by the applicant" In re Gurley, 27 F.3d at 553, 31 USPQ2d at 1131 (Fed. Cir. 1994). Here, Stolowitz explicitly states that 1,2,4-carbonyl di-triazole can be used as a substituted for CDI in similar types of coupling reactions (e.g., see Stolowitz et al., page 10, paragraph 1, "A variety of azolides other than N,N'-carbonyl-diimidazole [i.e., the coupling agent used by Jennissen] may be employed ... include[ing] N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonyldiindole, N,N,-carbonylidibenzimidazole and N,N'-carbonyldibenztriazole and others.").

Consequently, Stolowitz does not provide a "teaching away" or otherwise discredit Jennissen et al. as purported. If anything, Stolowitz stands for the proposition that CDI and 1,2,4-carbonyl di-triazole represent "equivalent" coupling reagents and, as a result, motivation to substitute one for another is not even required. See in In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982) ("Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious."). Furthermore, Stolowitz et al. state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30) and that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35; see also Stolowitz et al., page 4, lines 23-25), which further discredits Applicants' implication that the Stolowitz reference should somehow be limited to "the activation of silanized silica gel or controlled pore glass chromatographic supports and the covalent attachment of several functionalizing reagents" (e.g., see 6/29/06 response, page 15, last paragraph).

[4] An invention is "obvious to try" where the prior art provides either no indication of which parameters would be critical or no direction as to which of many possible choices is likely to be successful. Merck & Co. v. Biocraft Labs., Inc., 874 F.2d 804, 807, 10 USPQ2d 1843, 1845 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989) (quoting In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)).

This is not a situation where there are a large number of possibilities with no expectation of success. Stolowitz et al only list six azolides (e.g., see Stolowitz et al., page 10, paragraph 1). Furthermore, these compounds are structurally related to CDI and thus there is a presumed

expectation of success. See In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

Alternatively, the Examiner contends that Stolowitz et al. stands for the proposition that CDI and 1,2,4-carbonyl di-triazole represent "equivalent" coupling reagents (e.g., see Stolowitz et al., page 10, paragraph 1 as outlined above) and, as a result, motivation to substitute one for another need not be provided. See in In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982) ("Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious"). Therefore, Applicants' arguments are moot.

[5] This issue was adequately addressed in the response to the 35 U.S.C. § 102(b) rejection above, which is incorporated in its entirety herein by reference.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

9. Claims 1, 2, 4-13, 15, 18, 20-25, 27, 29, 32-34 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jennissen et al. (Jennissen et al., "Biocoating of Implants with Mediator Molecules: Surface Enhancement of Metals by Treatment with Chromosulfuric Acid" Mat.-wiss. u. Werkstofftech. 1999, 30, 838-845) and Stolowitz et al. (WO 87/06586) (Date of Publication is November 5, 1987) (of record) and Milton (US 6,146,833) (of record) and Okamoto et al. (US 6,476,215) (of record) and Guo et al. (Nuc. Acids Res. 1994, pp. 5456-5465) (of record) as evidenced by Madsen (Madsen, N. B. "Modification and characterization of the interface in polymer/inorganic composites" Risø National Laboratory, 1999, pages 3-6) and Zumbrink et al. (Zumbrink, et al. "Analysis of Affinity Supports by 13C CP/MAS NMR spectroscopy:

Application to Carbonyldiimidazole- and Novel Tresyl Chloride-Synthesized Agarose and Silica Gels" Journal of Molecular Recognition, 1995, 8, 363-373) and Bethell et al. (Bethell et al., "A Novel Method of Activation of Cross-linked Agaroses with 1,1'-Carbonyldiimidazole which Gives a Matrix for Affinity of Chromatography Devoid of Additional Charged Groups" J. Biol. Chem. 1979, 254(8), 2572-2574) and FDA (U.S. Food and Drug Administration "InFuse™ Bond Graft/LT-CAGE™ Lumbar tapered Fusion Device – P000058" September 2002, pages 1-3, accessed from http://www.fda.gov/cdrh/mda/docs/p000058.pdf).

For ***claims 1, 2, 4, 9-13, 15, 18, 29, 32 and 37***, the combined references of Jennissen et al. and Stolowitz et al. teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 1, 2, 4, 9-13, 15, 18, 29, 32 and 37.

For ***claim 21***, Jennissen et al. and Stolowitz et al. teach a "washing" step (e.g., (e.g., Jennissen et al., see page 840, column 2, paragraph 2).

The prior art combined teachings of Jennissen et al. and Stolowitz et al. differ from the claimed invention as follows:

For ***claims 5, 6, 22-23***, the prior art teachings of Jennissen et al. and Stolowitz et al. fail to recite the deposition of compounds in a particular area on the support (e.g., using inkjet printing).

For ***claims 7, 8, 24***, the prior art teachings of Jennissen et al. and Stolowitz et al. fail to recite the use of a humid chamber.

For ***claims 20, 27 and 33***, the prior art teachings of Jennissen et al. and Stolowitz et al. fail to recite a solid support selected from the group consisting of

cellulose, agarose, polypropylene, polystyrene, polymethacrylate, and nylon.

For ***claims 25 and 34***, the prior art combined teachings of Jennissen et al. and Stolowitz et al. fail to recite the use of an amino derivatized oligonucleotide.

However, the combined references of Milton et al. Okamoto et al. and Guo et al. teach the following limitations that are deficient in Jennissen et al. and Stolowitz et al.:

For ***claims 5, 6, 22-23***, However, the use of printing techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, (e.g., see for example, Milton et al. column 12, lines 24-41; see also column 8, line 33; see also column 11, line 62; see also column 17, line 2; see also Guo et al., page 5457, column 1; see also Okamoto et al., columns 1-3). The reference teaches methods for printing compounds to make an array (e.g., see Milton, Examples 5 and 6 wherein spot diameter is, for example, 250 μm; note this procedure is referred to in the instant specification, pages 9 and 10; see also Milton, Examples 3-9 wherein immobilization of oligonucleotides and peptides is taught).

For ***claims 7, 8 and 24***, the combined references of Milton, Okamoto et al. and Guo et al further teach a humid chamber during the attachment of the probes to their arrays (e.g., see Guo, page 5457, column 1; see also Okamoto et al., column 18, lines 42-46). This step is used to complete the reaction and/or to incubate the arrays.

For ***claims 20, 27 and 33***, the combined references of Milton, Okamoto et al. and Guo et al. disclose, for example, polypropylene including "aminated" polypropylene (e.g., see Milton, column 2, line 5; see also column 6, last paragraph; see also figures 1, 6, 10, 14; see also Examples; see also claims 2, 4, 8 and 11; see also figures 1-7; see also

column 2, lines 5-8 wherein glass slides, polymer films, silicon wafers are disclosed; see also column 2, lines 47-50; see also column 3, line 4; and claim 23).

For ***claim 21***, the combined references of Milton, Ocamoto et al. and Guo et al. also disclose a "washing" step (e.g., see Example 5).

For ***claims 25 and 34***, the combined references of Milton, Okamoto et al. and Guo et al. further teach the use of amino derivatized oligonucleotides with one free amino (e.g., see Milton, Detailed Description of Invention, "For example, designed DNA libraries consisting of site-specific arrays of oligonucleotides of known sequence immobilized to a solid support surface have utility in detecting individual genetic mutations using reverse hybridization techniques"; see also columns 10-11, "The following shows a generalized reaction between an amino derivatized oligonucleotide and a solid support surface").

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use the carbonyl diimidazole (CDI) immobilization chemistry and related compounds such as 1,2,4-carbonyl di-triazole as taught by the combined references of Jennissen et al. and Stolowitz et al. in an array-type format using a "printing method" to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by Milton, Guo and Okamoto because "immobilization" of biomolecules is required in each case (i.e., the references represent analogous art). One of ordinary skill would have been motivated to do so in order to create covalently attached amine bound biomolecules "immobilized at site specific locations" as taught by Milton (for example). In addition, a person of skill in the art would have been motivated to use a "humid chamber" to complete

the reaction and/or to incubate the arrays once created.

In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to immobilize affinity ligands in an array format for analytical and diagnostic purposes as taught by the combined references of Milton, Okamoto et al. and Guo et al. (e.g., see Milton et al., abstract) using the CDI/1,2,4-carbonyl di-triazole immobilization procedures as taught by the combined references of Jennissen et al. and Stolowitz et al. because Stolowitz et al., for example, explicitly state that CDI/1,2,4-carbonyl di-triazole can be used for this purpose (e.g., see Stolowitz, column 6, lines 43-56, "An 'affinity ligand' ... may also be used as a diagnostic reagent ... [which] permits the detection and/or quantitation of such biological molecules"; see also lines 23-26, "'the chromatographic material containing the affinity ligand may comprise ... the inner surface of a microtitre plate [i.e., an array]"). Furthermore, one of ordinary skill in the art would have been motivated to use the CDI immobilization techniques as taught by the combined teachings of Jennissen et al. and Stolowitz et al. because Stolowitz et al., for example, explicitly state that they obtain "near quantitative derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30). Stolowitz et al. also state that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35). In addition, the combined references of Jennissen et al. and Stolowitz et al. state that their method provides for a physical barrier that decreases non-specific binding that might otherwise interfere with an analytical and/or diagnostic assay (e.g., see Stolowitz et al., page 4, lines 11-19, "The preparation of

a physical barrier preventing interaction between surface silanols and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and sample components; and the functionalization of the physical barrier to impart properties resulting in selective retention of sample components"; see also page 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the residual silanol activity beneath it"), which the combined teachings of Milton, Okamoto et al. and Guo et al. recognize as being "crucial" for the proper operation of their diagnostic arrays (e.g., see Milton, column 6, lines 38-43, "This [non-specific binding] is an important consideration because diagnostic applications which depend upon detecting reagents specifically bound to biopolymers immobilized to solid supports cannot tolerate nonspecific binding to the solid support").

Finally, one of ordinary skill in the art would have reasonably expected to be successful because Stolowitz et al. also state, "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" and Jennissen et al. provide a specific example of a protein, which would encompass the proteins disclosed by Milton (see Milton, column 11, lines 28-30, "Similarly any protein or peptide with surface amino groups, e.g. lysine can be immobilized to a solid support"; see also Stolowitz et al., page 4, lines 34-35). In addition, all references teach the use of CDI for immobilization (e.g., compare Jennissen et al. (e.g., page 840, column 2, paragraph 1 wherein CDI is disclosed) to Milton (e.g., see column 8, lines 37-55, "In another aspect, the present invention provides methods for preparing reagents for immobilizing biopolymers which

include providing a solid support fabricated of ethylene acrylic acid copolymer or ethylene methacrylic acid copolymer and derivatizing at least one surface of the solid support by reacting the surface with an activating agent. Suitable activating agents are ... carbodiimides"; see also Example 9 wherein the use of diisopropylcarbodiimide is disclosed).

Response

10. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "[a]s detailed above ... Jennison et al. is non-analogous art" (e.g., see 6/29/06 response, page 17, last full paragraph).

[2] Applicants argue that the claims are non-obvious "for the reasons stated in paragraphs VI(A)(1-2) above" (e.g., see 6/29/06 response, paragraph bridging pages 17 and 18).

[3] Applicants argue that the Examiner was "factually incorrect" when he stated that CDI could be used to immobilize ligands (e.g., see 6/29/06 response, page 18, section a).

[4] Applicants again set forth the same argument that Jennison et al. and Stolowitz et al. fail to provide ligands "for use" as "diagnostic reagents" (e.g., see 6/29/06 response, page 18, last paragraph).

[5] Applicants argue that there is no motivation to combine the derivatized polypropylene

films of Milton with the activating compounds disclosed in Jennison or Stolowitz (e.g., see 6/29/06 response, page 19, paragraph 1).

[6] Applicants argue none of the cited references teach or suggest forming an "activated support" as currently claimed (e.g., see 6/29/06 Response, page 19, last two paragraphs).

[7] Applicants argue that none of the cited references teach the use of the recited Markush of solid supports including cellulose, agarose, polypropylene, polystyrene, polymethacrylate and nylon in accordance with claims 20-25 and 27 (e.g., see 6/29/06 Response, page 20, paragraphs 1 and 2).

[8] Applicants argue that none of the recited references teach Applicants' "two step" process (e.g., see 6/29/06 Response, page 20, paragraph 2).

[9] Applicants argue that Example 9 of Milton does not teach their claimed invention and, more specifically, that Milton fails to teach the use of a CDI activated solid support (e.g., see 6/29/06 Response, page 20, last two paragraphs).

[10] Applicants again argue that Jennissen teaches away from the claimed invention. Specifically, Applicants state that Jennissen teaches away from the use of CDI in a biological assay because non-specific binding would occur, which is not favorable for diagnostic assays (e.g., see 6/29/06 Response, page 21).

[11] Applicants argue that Milton also teaches away from the claimed invention (e.g., see 6/29/06 Response, pages 22 and 23). Specifically, Applicants argue that (1) activation of oligonucleotides with CDI is unstable (and cite column 1, lines 43-56 in support of this position), (2) the use of CDI creates unwanted urea side products when said CDI is used in an organic solvent (and cite claim 9 in support of this position), and that Milton teaches only acyl fluoride

functionalities because the block groups on the propylene films that are not carboxylated (and cite column 17, line 9 to column 18 line 4).

[12] Applicants again argue that Jennissen teaches away from the claimed invention because it shows non-specific binding that, according to Applicants, originated from the use of CDI, which would not be favorable for the application disclosed by the other references including Milton (e.g., see 6/29/06 Response, page 23, paragraphs 1 and 2).

[13] Applicants argue that the claimed 1,2,4-carbonyl di-triazoles as set forth in claims 4, 15 and 37 exhibit "unexpected results" for attaching biological molecules and cite the test results shown in Examples 2 and 3 of the specification in support of this position which, according to Applicants, shows "increased oligonucleotide loading" and "higher sensitivity" for analyte detection that the prior art acyl fluoride (AcF) method, an example of the method disclosed in Milton, and a CDI method, as taught by Hermanson et al. (e.g., see 6/29/06 Response, page 24).

This is not found persuasive for the following reasons:

[13] An applicant bears the burden of proving unexpectedly good results. In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). When unexpected results are used as evidence of non-obviousness, the results must be shown to be unexpected compared with the closest prior art. *In re Baxter Travenol Labs*, 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196, (Fed. Cir. 1984). In the present case, Examples 2 and 3 cited by Applicants fail to provide a comparison with the closest prior art of record, Stolowitz, which discloses, for example, N,N'-carbonyldi-1,2,3-triazole, (e.g., see Stolowitz et al., page 10, paragraph 1). Consequently, Applicants failed to meet their burden of proving unexpected results with the closest prior art. Furthermore, the Examiner notes that

1,2,4-carbonyl di-triazole was also disclosed by the prior art rendering this argument moot (e.g., see Stolowitz et al., page 10, paragraph 1).

[1] To the extent that Applicants are merely repeating their "non-analogous" arguments, the Examiner contends that those arguments were adequately addressed in the previous 35 U.S.C. § 103(a) response (e.g., sections [1,6]), which are incorporated in their entirety herein by reference.

[2] To the extent that Applicants are merely repeating their previous arguments, the Examiner contends that those arguments were adequately addressed in the previous 35 U.S.C. § 103(a) response (e.g., sections [2-5]), which are incorporated in their entirety herein by reference.

[3] The Examiner respectfully disagrees. CDI was a commonly used in the art to immobilize ligands to a solid support in many different fields of research as evidenced by the combined teachings of Jennissen et al., Stolowitz et al., Milton, Okamoto et al. and Guo et al. as outlined above. For example, Jennissen et al. teach the use of CDI to for Ti-APS-CDI plates for the immobilization of ubiquitin and rhBMP (e.g., see page 840, column 2, paragraph 2; see also page 840, column 2, last paragraph wherein ubiquitin is used to form Ti-APS-CDI-ubiquitin plates; see also page 841, column 1, paragraph 1 wherein rhBMP is used to form Ti-APS-CDI-rhBMP plates). Likewise, Stolowitz also disclose that CDI and various other coupling reagents were commonly used to immobilize ligands onto substrates (e.g., see Stolowitz et al., page 10, paragraph 1, "A variety of azolides other than N,N'-carbonyl-diimidazole [i.e., CDI] may be employed ... include[ing] N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonyldiindole, N,N,-carbonylidibenzimidazole and N,N'-

carbonyldibenztriazole and others"). In addition, Stolowitz explicitly states that such immobilization can be used for "diagnostic purposes" (e.g., see Stolowitz, column 6, lines 43-56, "An 'affinity ligand' ... may also be used as a diagnostic reagent ... [which] permits the detection and/or quantitation of such biological molecules"; see also lines 23-26, "'the chromatographic material containing the affinity ligand may comprise ... the inner surface of a microtitre plate [i.e., an array]").

[4] In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "diagnostic reagents") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In addition, the limitation "so that the biological molecule is available for use in an assay" has not been afforded any patentable weight for the reasons outlined above and, as a result, Applicants' arguments are moot.

[5] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art would have been motivated to use the CDI immobilization techniques as taught by the combined teachings of Jennissen et al. and Stolowitz et al. because Stolowitz et al., for example, explicitly state that they obtain "near quantitative

derivatization of bonded supports ... by this synthetic route" (e.g., see Stolowitz et al., page 4, lines 29-30). Stolowitz et al. also state that their method is "versatile" because "almost [an] infinite variety of ligands ... can be employed as functionalizing reagents" (e.g., see Stolowitz et al., page 4, lines 34-35). In addition, the combined references of Jennissen et al. and Stolowitz et al. state that their method provides for a physical barrier that decreases non-specific binding that might otherwise interfere with an analytical and/or diagnostic assay (e.g., see Stolowitz et al., page 4, lines 11-19, "The preparation of a physical barrier preventing interaction between surface silanols and sample components; The derivatization of the physical barrier preventing interaction between the hydrophobic silane backbone and sample components; and the functionalization of the physical barrier to impart properties resulting in selective retention of sample components"; see also page 7, first full paragraph, "The urea linkage ... is uncharged under normal chromatographic conditions and provides a hydrophilic barrier masking the properties of the silane backbone and the residual silanol activity beneath it"), which the combined teachings of Milton, Okamoto et al. and Guo et al. recognize as being "crucial" for the proper operation of their diagnostic arrays (e.g., see Milton, column 6, lines 38-43, "This [non-specific binding] is an important consideration because diagnostic applications which depend upon detecting reagents specifically bound to biopolymers immobilized to solid supports cannot tolerate nonspecific binding to the solid support").

[6] The Examiner respectfully disagrees. Jennissen et al., for example, disclose the titanium-APS-CDI, which represents and "activated support" as defined by Applicants' newly amended claims. In this case, the free amine of the APS reacts with the CDI by displacing one of the imidazole rings (i.e., the L_1 is displaced). Therefore, Applicants' arguments are moot.

[7] As outlined in detail above, the combined references do teach members of the recited Markush. For example, the combined references of Milton, Okamoto et al. and Guo et al. disclose polypropylene including "aminated" polypropylene (e.g., see Milton, column 2, line 5; see also column 6, last paragraph; see also figures 1, 6, 10, 14; see also Examples; see also claims 2, 4, 8 and 11; see also figures 1-7; see also column 2, lines 5-8 wherein glass slides, polymer films, silicon wafers are disclosed; see also column 2, lines 47-50; see also column 3, line 4; and claim 23).

[8] In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "two-step" process) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, Applicants' use of "comprising" language would not preclude additional method steps (i.e., a three step process). Furthermore, the combined references do teach a two step process (e.g., see Jennissen et al., page 840, column 2, paragraph 1).

[9] In response to applicant's arguments against the Milton reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, the combined references teach all of the claimed limitations as outlined above.

[10, 12] As noted above, the phrase "so that the biological molecule is available for use in an assay" has not been afforded any patentable weight (e.g., see newly amended rejection above)

and, as a result, Applicants' arguments are moot. Alternatively, the Examiner contends that Stolowitz et al. stands for the proposition that CDI and 1,2,4-carbonyl di-triazole represent "equivalent" coupling reagents (e.g., see Stolowitz et al., page 10, paragraph 1 as outlined above) and, as a result, motivation to substitute one for another need not be provided. See in In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982) ("Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious"), which again renders Applicants' arguments moot. Finally, the Examiner notes that Stolowitz et al., not Jennissen, teach the alleged criticality of preventing non-specific binding and it is the Stolowitz et al. reference that expressly endorses the use of CDI (e.g., see Stolowitz et al., page 10, paragraph 1, "A variety of azolides other than N,N'-carbonyl-diimidazole [i.e., CDI] may be employed ... include[ing] N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonyldiindole, N,N,-carbonylidibenzimidazole and N,N'-carbonyldibenztriazole and others." If CDI was viewed as Applicants' allege to cause an increase in non-specific binding, Stolowitz et al. never would have listed this reagent as a preferred embodiment. Furthermore, the Stolowitz et al. reference explains that the use of CDI would reduce non-specific binding because a "urea" linkage would be formed when said CDI reacts with free amines (e.g., see Stolowitz et al., page 9, formula 7 wherein the urea linkage is shown; see also Summary of Invention, "In addition, a number of important specific objectives are also achieved using the present invention, including: The use of N,N'-carbonyldiimidazole for the activation of a chromatographic support with other than pendant hydroxyl groups; The preparation of a urea derivative of a bonded phase chromatographic support and the unique hydrophilic nature of the urea linkage"). Finally, the Examiner notes that a reference that

"teaches away" does not per se preclude a prima facie case of obviousness, but rather the "teaching away" of the reference is a factor to be considered in determining unobviousness. Id 27 F.3d at 552, 31 USPQ 2d at 1132. Here, even if, assuming arguendo, Jennissen et al. teaches away from the claimed invention (which is not the case, see above), that would not overcome the prima facie case of obviousness for the reasons set forth above.

[11] The test to determine if a reference "teaches away" is to determine if one "would be discouraged from following the path set out in the reference, or would be lead in a direction divergent from the path that was taken by the applicant" *In re Gurley*, 27 F.3d at 553, 31 USPQ2d at 1131 (Fed. Cir. 1994). Here, Applicants' arguments fail to appreciate that the combined references teach more than the use of CDI in an organic solvent. Thus, the combined references, when viewed in their entirety, do not "teach away" from the claimed invention. For example, Stolowitz et al. teach the use of 1,2,4-carbonyl di-triazole (e.g., see Stolowitz et al., page 10, paragraph 1) to which Applicants' cited passages are not applicable. That is, Applicants have not even argued that the references "teach away" from the use of 1,2,4-carbonyl di-triazole. Consequently, Applicants' arguments are not commensurate in scope with the claims. In addition, the claims do not require the "activation" of the biological molecule but, rather, activation of the solid support and, as a result, Applicants' argument concerning activation of the biological molecule is not on point (i.e., the column 1, lines 43-56 citation). Furthermore, the claims do not require that the CDI be used in the presence of an organic solvent (as allegedly) and, as a result, Applicants' arguments are again not commensurate in scope with the claimed invention. Furthermore, Applicants' argument with regard to the "blocking" groups on the propylene films is less than clear. For example, Stolowitz et al. also state, "almost [an] infinite

variety of ligands ... can be employed as functionalizing reagents" and Jennissen et al. provide a specific example of a protein, which would encompass the proteins disclosed by Milton (see Milton, column 11, lines 28-30, "Similarly any protein or peptide with surface amino groups, e.g. lysine can be immobilized to a solid support"; see also Stolowitz et al., page 4, lines 34-35). Consequently, it is unclear how the use of "blocking" groups subtracts from this teaching. In addition, all of the references explicitly teach the use of CDI for immobilization (e.g., see Jennissen et al., page 840, column 2, paragraph 1 disclosing the use of CDI; see also Milton, column 8, lines 37-55, "In another aspect, the present invention provides methods for preparing reagents for immobilizing biopolymers ... Suitable activating agents are ... carbodiimides"; see also Example 9; see also see also Stolowitz et al., page 10, paragraph 1, "A variety of azolides other than N,N'-carbonyl-diimidazole [i.e., CDI] may be employed"). Therefore, Applicants' argument that Milton should somehow be limited to the use acyl fluorides is not supported in fact.

Finally, the Examiner notes that a reference that "teaches away" does not *per se* preclude a *prima facie* case of obviousness, but rather the "teaching away" of the reference is a factor to be considered in determining unobviousness. Id 27 F.3d at 552, 31 USPQ 2d at 1132. Here, Stolowitz et al., for example, explicitly state that CDI/1,2,4-carbonyl di-triazole can be used for "diagnostic" tests in an "array" format (e.g., see Stolowitz, column 6, lines 43-56, "An 'affinity ligand' ... may also be used as a diagnostic reagent ... [which] permits the detection and/or quantitation of such biological molecules"; see also lines 23-26, "'the chromatographic material containing the affinity ligand may comprise ... the inner surface of a microtitre plate [i.e., an array]"), which would outweigh any alleged inconsistencies noted for the Milton reference.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

New Rejections

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 2, 4-13, 15, 18, 29, 32-34 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claims 1, 12, 29 and 37**, the term "consisting essentially of and organic polymer" is vague and indefinite because it is unclear what components could be added to the organic polymer without affecting the basic and novel characteristic of the polymer in light of the prosecution history. For example, although the specification and claims make clear that a free amino group is required (e.g., see currently amended claim 1, step (a)), it is unclear how the addition of the addition of a titanium layer (as in the Jennissen et al. reference, see page 840, column 2, paragraph 1) would alter the basic and novel characteristics of the APS polymer because it does not prevent in any way the free amino groups from reacting with the CDI. In addition, Applicants' attempt to distinguish the Jennissen et al. reference based on this newly added limitation does not clarify the issue because they never mention what characteristics they are relying on to support this

position (e.g., see 6/29/06 Response, page 12, section IV). Therefore, claims 16, 19, 23 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 2, 4-13, 15, 18, 29, 32-34 and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claims 1, 12, 29 and 37 added the new limitation "consisting essentially" of an organic polymer. However, applicant did not show where support for this new subgenus of solid supports could be found in the specification. If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02. Therefore, claim 1, 12, 29, 37 and all dependent claim are rejected for containing new matter.

Claim Rejections - 35 USC § 103

13. Claims 1, 2, 9, 11-13, 18, 20, 21, 25, 27, 29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abbott et al. (U.S. Patent Application No. 2002/0055093 A1) (earliest U.S. Priority **Feb 16, 2000**) in view of Haginaka et al. (Haginaka et al. "Retention and enantioselectivity of 2-arylpropionic acid derivatives on an avidin-bonded silica column

Influence of base materials, spacer type and protein modification" *J. Chromatogr.* **1994**, *677*, 229-237) as evidenced by Madsen (Madsen, N. B. "Modification and characterization of the interface in polymer/inorganic composites" Risø National Laboratory, 1999, pages 3-6) and Ganne (U.S. Patent No. 6,689,370) (Filing date is **November 28, 2000**).

For ***claims 1 and 12***, Abbott et al. (see entire document) teach a method for immobilizing BSA on a solid support (e.g., see abstract; see also figure 1), which reads on the claimed invention. For example, Abbott et al. teach **(a)** providing a solid support consisting essentially of an organic polymer having at least one available amino group (e.g., see figure 1 showing APES polymer with at least one amino group). The reference doesn't explicitly state that APS forms an organic polymer, but the Examiner contends that Abbott et al. inherently discloses this feature as evidenced by Madsen (e.g., see Madsen, page 5, figure 1.2 showing polymerization of organosilanes and their subsequent attachment to free hydroxyl groups; see also Jennissen et al., page 840, column 2, paragraph 1). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). In addition, Abbott et al. explicitly recite the use of an organic polymer (e.g., see page 6, column 2, paragraph 1). In addition, Abbott et al. disclose **(b)** the use of an activating agent N,N'-disuccinimidyl suberate DSS with a L1-X-L2 structure (i.e., L1 & L2 = N-

oxy-1H-pyrrole-2,5-dione and X = -(C=O)-$(CH_2)_6$-(C=O)-, note differences below) wherein L1 is displaced during the course of the reaction with the available amino group to form an activated support (e.g., see figure 1, "Activation of Surface with DSS). Furthermore, Abbott et al. disclose **(c)** a method step for providing a biological molecule having at least one reactive amino, thiol, or hydroxyl group, the biological molecule being a macromolecule selected from the group consisting of nucleic acids, polypeptide chains, and carbohydrates (e.g., see figure 1 showing BSA with a free amino group). Finally, Abbott et al. disclose **(d)** reacting the biological molecule with the activated support thereby displacing L2 and covalently attaching the biological molecule to the solid support so that the biological molecule is available for use in an assay (e.g., see figure 1, last step showing attachment; see also abstract showing its availability for use in an assay).

For ***claim 9***, Abbot et al. disclose the use of an organic solvent like DMSO (e.g., see paragraph 87).

For ***claim 11***, Abbott et al. disclose the use of phosphate buffer (e.g., see paragraph 87).

For ***claims 18 and 21***, Abbott et al. disclose washing with methanol (e.g., see paragraph 87).

For ***claims 20 and 33***, Abbott et al. also disclose cellulose, polystyrene, and polymethacrylate (e.g., see page 6, column 2, paragraph 1).

For ***claim 25***, Abbott et al. disclose the use of a free amino group (e.g., see figure 1 showing "NH_2" on BSA).

For ***claim 29***, Abbott et al. do not explicitly state that BSA can act as a therapeutic drug, but the Examiner contends that this is an inherent property of BSA as evidenced by Ganne (see Example 1, "Therapeutic compositions (or doses) of 100 pl each, comprising 50 pg of BSA, are prepared.").

The prior art teachings of Abbott et al. differ from the claimed invention as follows:

For ***claims 1, 2, 9, 11-13, 18, 20, 21, 25, 27, 29 and 33***, Abbott et al. fail to disclose the recited X in the formula L1-X-L2. As noted above, Abbott et al. only disclose X = -(C=O)-$(CH_2)_6$-(C=O)- which does not fall within the scope of the recited Markush of X groups.

For ***claims 2 and 13***, Abbott et al. fail to disclose the recited Markush listing of L1 and L2 groups.

However, Haginaka et al. teach the following limitations that are deficient in Abbott et al.:

For ***claim 1***, Haginaka et al. (see entire document) teach the use of X = C=O (e.g., see abstract wherein N,N'-disuccinimidyl carbon DSC is disclosed).

For ***claims 2, 13***, Haginaka et al. disclose, for example, the use of CDI that contains an imidazole ring (e.g., see abstract).

For ***claim 9***, Haginaka et al. additionally disclose the use of an organic solution such as acetonitrile or dioxane (e.g., Haginaka et al., page 230, column 2, last paragraph).

For ***claim 11***, Haginaka et al. additionally disclose the use of phosphate buffer (e.g., see page 231, column 1, paragraph 1).

For ***claims 18, 21***, Haginaka et al. additionally disclose washing with acetonitrile and methanol (e.g., see page 230, column 2, last paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make substitute the DSC as taught by Haginaka et al. in place of the DSS as taught by Abbott et al. because Haginaka et al. explicitly state that these two coupling reagents can be used interchangeable to effectuate coupling of a protein such as avidin to a solid support (e.g., see abstract; see also page 230, column 2, last paragraph; see also page 231, column 1; see also page 232, sections 3.1 and 3.2; see also Table 1). Furthermore, a person of ordinary skill in the art would have been motivated to use the DSC reagent because Haginaka et al. state that this reagent produces higher surface coverage than DSS and is more stable than other coupling reagents like CDI. In addition, the DSC would reduce the amount of non-specific binding with the alkyl linker chain (e.g., see Haginaka et al., section 3.2). Finally, one of ordinary skill in the art would have reasonably expected to be successful because Haginaka et al. teach that both DSS and DSC can be used interchangeably to attach a protein to a solid support including solid supports that contain free amino groups (e.g., see page 230, column 2, "Activation of silica gels having amino or hydroxyl groups") like the free amino groups disclosed by Abbott (e.g., see figure 1).

Alternatively, the Examiner contends that Haginaka et al. stands for the proposition that CDI, DSS and DSC represent "equivalent" coupling reagents (e.g., see abstract) and, as a result, motivation to substitute one for another is not needed to render the claimed invention obvious. See *In re Fout*, 675 F.2d 297, 301, 213 USPQ 532, 536

(CCPA 1982) ("Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious").

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
August 17, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER